Appl. No. 09/432,503 Amdt. dated May 5, 2004 Supplemental Reply to Advisory Action of March 19, 2004

Amendments to the Specification:

Please note that the following amendments are made in reference to the <u>substitute specification</u> filed February 25, 2003.

Please replace the paragraph beginning at page 12, line 12, with the following rewritten paragraph:

--Figure 13, in two pages, shows Figures 13A and 13B show the sequence of the DNA encoding the Euplotes 123 kDa telomerase protein subunit (Euplotes TRT; SEQ ID NO:109).--

Please replace the paragraph beginning at page 12, line 16, with the following rewritten paragraph:

--Figure 15, in five pages, shows Figures 15A-15F show the DNA (SEQ ID NO:111) and amino acid (SEQ ID NO:112) sequences of the *S. pombe* telomerase catalytic subunit (*S. pombe* TRT).--

Please replace the paragraph beginning at page 12, line 26, with the following rewritten paragraph:

--Figure 20 shows, in seven pages, Figures 20A-20E show the sequence of a nucleic acid with an open reading frame encoding a $\Delta 182$ variant polypeptide, with the sequence shown corresponding to SEQ ID NO:4. This Figure also shows the amino acid sequence of this $\Delta 182$ variant polypeptide, with the amino acid sequence shown corresponding to SEQ ID NO:5.

Please replace the paragraph beginning at page 12, line 30, with the following rewritten paragraph:

--Figure 21 shows, in six pages, Figures 21A-21E show sequence from an hTRT genomic clone, with the sequence shown corresponding to SEQ ID NO:6. Consensus motifs and elements are indicated, including sequences characteristic of a topoisomerase II cleavage site, NFκB binding sites, an Alu sequence and other sequence elements.--

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Please replace the paragraph beginning at page 14, line 3, with the following rewritten paragraph:

--Figure 35 shows, in four pages, Figures 35A-35D show the DNA sequence (SEQ ID NO:115), as well as the amino acid sequences of all three open reading frames of the 43 kDa telomerase protein subunit from *Euplotes* (a = SEQ ID NOS:116-140; b = SEQ ID NOS:141-162; c = SEQ ID NOS:163-186).--

Please replace the paragraph beginning at page 14, line 7, with the following rewritten paragraph:

--Figure 36 shows Figures 36A and 36B show a sequence comparison between the 123 kDa telomerase protein subunit of *Euplotes* (SEQ ID NO:187) (upper sequence) and the 80 kDa polypeptide subunit of *T. thermophila* (SEQ ID NO:188) (lower sequence).--

Please replace the paragraph beginning at page 14, line 10, with the following rewritten paragraph:

--Figure 37 shows Figures 37A and 37B show a sequence comparison between the 123 kDa telomerase protein subunit of *E. aediculatus* (SEQ ID NO:189) (upper sequence) and the 95 kDa telomerase polypeptide of *T. thermophila* (SEQ ID NO:190) (lower sequence).--

Please replace the paragraph beginning at page 15, line 19, with the following rewritten paragraph:

--Figure 52 shows, in two pages, Figures 52A and 52B show the DNA sequence of *tez1* (SEQ ID NO:111). Intronic and other non-coding regions are shown in lower case and exons (*i.e.*, coding regions) are shown in upper case.--

Please replace the paragraph beginning at page 16, line 4, with the following rewritten paragraph:

--Figure 58 shows Figures 58A and 58B show the alignment of the M2 PCR product (SEQ ID NO:243) with *E. aediculatus* p123 (SEQ ID NO:242), *S. cerevisiae* (SEQ ID NO:244), and *Oxytricha* (SEQ ID NO:223) telomerase protein sequences. Also shown are the actual genomic sequences (SEQ ID NOS:246 and 249) and the peptides encoded (SEQ ID NOS:245 and 250), degenerate primers Poly4 (SEQ ID NO:238) and Poly 1 (SEQ ID NO:244),

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and homologous regions of the M2 PCR product (SEQ ID NO:247) and its encoded peptide region (SEQ ID NO:248).--

Please replace the paragraph beginning at page 16, line 24, with the following rewritten paragraph:

--Figure 64 shows Figures 64A-64J show the alignment of the sequences from Euplotes ("Ea_p123") (SEQ ID NO:110), S. cerevisiae ("Sc_Est2p") (SEQ ID NO:222), and S. pombe ("SP_Tlplp") (SEQ ID NO:112). In Panel A, the shaded areas indicate residues shared between two sequences. In Panel B, the shaded areas indicate residues shared between all three sequences.--

Please replace the paragraph beginning at page 17, line 1, with the following rewritten paragraph:

--Figure 68 shows, in four pages, Figures 68A-68C show the DNA (SEQ ID NO:266) and amino acid (SEQ ID NO:267) of the ORF encoding an approximately 63 kDa telomerase protein encoded by the EcoRI-NotI insert of clone 712562.--

Please replace the paragraph beginning at page 17, line 9, with the following rewritten paragraph:

--Figure 71 shows, in two pages, Figures 71A and 71B show the results of preliminary nucleic acid sequencing analysis of a hTRT cDNA sequence (SEQ ID NO:292).--

Please replace the paragraph beginning at page 17, line 11, with the following rewritten paragraph:

--Figure 72 shows, in ten pages, Figures 72A-72I show the preliminary nucleic acid sequence of hTRT (SEQ ID NO:292) and deduced ORF sequences in three reading frames (a = SEQ ID NOS:293-320; b = SEQ ID NOS:321-333; c = SEQ ID NOS:334-342).--

Please replace the paragraph beginning at page 17, line 15, with the following rewritten paragraph:

--Figure 74 shows, in eight pages, Figures 74A-74F show refined nucleic acid sequence (SEQ ID NO:343) and deduced ORF sequences (SEQ ID NO:344) of hTRT.--

Amendments to the Drawings:

The attached sheets of drawings include changes to the following drawings as indicated below:

- Fig. 13 (2 sheets) are replaced with attached sheets Figs. 13A and 13B;
- Fig. 15 (6 sheets) are replaced with attached sheets Figs. 15A-15F;
- Fig. 20 (5 sheets) are replaced with attached sheets Figs. 20A-20E;
- Fig. 21 (5 sheets) is replaced with attached sheets Figs.21A-21E;
- Fig. 35 (4 sheets) are replaced with attached sheets Figs. 35A-35D;
- Fig. 36 (2 sheets) are replaced with attached sheets Figs. 36A and 36B;
- Fig. 37 (2 sheets) are replaced with attached sheets Figs. 37A and 37B;
- Fig. 52 (2 sheets) are replaced with attached sheets Figs. 52A and 52B;
- Fig. 58 (2 sheets) are replaced with attached sheets Figs. 58A and 58B;
- Fig. 64 (10 sheets) are replaced with attached sheets Figs. 64A-64J;
- Fig. 68 (3 sheets) are replaced with attached sheets Figs. 68A-68C;
- Fig. 71 (2 sheets) are replaced with attached sheets Figs. 71A and 71B;
- Fig. 72 (9 sheets) are replaced with attached sheets Figs. 72A-72I; and
- Fig. 74 (6 sheets) are replaced with attached sheets Figs. 74A-74F.

Attachment: Replacement Sheets